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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/832,320	04/10/2001	Edmund H. Crane III	35718/214291 (5718-183)	8792

27310 7590 03/27/2003

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/832,320	Applicant(s) CRANE ET AL.	
	Examin r Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-8 and 10-13, in Paper No. 9 is acknowledged. Claim 9 is withdrawn from consideration as being drawn to a non-elected invention.

2. The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. See pg 26, line 15 and pg 27, line 26. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

3. The abstract is not descriptive of the instant invention, which is a maize PR1-C10 nucleic acid with 50-60% identity to maize PR1 genes, vectors and expression cassettes comprising those nucleic acids, cells, plants and seeds comprising the vector, and a method of using the expression cassette to modulate the level of PR1-C10 in a plant. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

4. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

Claim Objections

5. Claims 1-3 and 10-11 are objected to because of the following informalities:

In claim 1, part (g) and claim 10, part (vii), there is an improper article before the second recitation of "polynucleotide".

In claim 2 "claim1" should be replaced with --claim 1--.

There is an improper article before "nucleic" in claim 3, line 1.

In claim 11, --the group consisting of-- should be inserted after "from".

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a nucleic acid with 85% identity to SEQ ID NO:1 or 3, a nucleic acid comprising 20 contiguous nucleotides of SEQ ID NO:1 or 3, or a nucleic acid that hybridizes to SEQ ID NO:1 or 3, vectors and expression cassettes comprising those nucleic acids, cells, plants and seeds comprising the vector, and a method of using the expression cassette to modulate the level of PR1-C10 in a plant.

The instant specification, however, only provides guidance for identification of a maize PR1-C10 nucleic acid while sequencing a clone in a randomly selected maize cDNA library; the clone was used to probe a lambda library to isolate a full-length clone (example 1). The clone (SEQ ID NO:1, the coding region of which, SEQ ID NO:3, encodes SEQ ID NO:2) was identified as encoding PR1 protein by its having 50-60% identity to maize PR1 genes (example 2). Maize PR1-C10 gene expression was analyzed by Northern analysis to show that elicitor or

spore treatment does not induce its expression and the RNA is abundant in R1 leaf-blade joints (example 3). The specification also provides general guidance for maize, soybean and sunflower transformation (examples 4-6).

The instant specification fails to provide guidance for a nucleic acid with 85% identity to SEQ ID NO:1 or 3, a nucleic acid comprising 20 contiguous nucleotides of SEQ ID NO:1 or 3, or a nucleic acid that hybridizes to SEQ ID NO:1 or 3, vectors and expression cassettes comprising those nucleic acids, cells, plants and seeds comprising the vector, and a method of using the expression cassette to modulate the level of PR1-C10 in a plant.

For example, the instant specification fails to provide guidance for the exact hybridization or amplification conditions and probes/primers to use in the isolation of nucleic acids other than SEQ ID NOs:1 and 3.

The specification also fails to provide adequate guidance for making those nucleic acids. The specification suggests making mutations that result in conservative substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) in the protein (pg 59, line 20, to 61, line 23), but this does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). Thus, without specific guidance as to which amino acids

to modify, substitutions cannot be reliably made in proteins.

The specification provides no assay for "PR1-C10 activity" and it is not clear what this activity is. Pg 39, lines 27-29, of the specification provides examples of PR1-C10 like activity, as participation in the pathogenic response and enhancement of disease resistance, but PR1-C10 like activity is not defined and the nature of the participation or enhancement is not detailed. A great many proteins participate in the pathogenic response and enhance disease resistance, but these proteins have very different specific activities (Delaney, 1997, Plant Physiol. 113:5-12, see Table 1 and Figure 2). The specification does not teach which of these, or other possible activities with a role in the pathogenic response and disease resistance, is PR1-C10-like activity.

It is not clear that the instant nucleic acid actually encodes a protein that participates in the pathogenic response and enhances disease resistance. The instant specification states that SEQ ID NO:1 has only 50-60% identity to maize PR1 genes. The specification provides no evidence that SEQ ID NO:1 actually encodes a protein with PR1 activity, and the lack of activation in response to elicitor or spore treatment suggests that SEQ ID NO:2 does not play a role in pathogen defense. Duggleby (1997, Gene 190:245-249) teach that "the function of any DNA sequence, whose identity is based solely on homology, can only be proven by experiments designed to evaluate that function" (pg 248, left column, paragraph 4).

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids with 85% identity to SEQ ID NOs:1 or 3. Making all possible single amino acid substitutions in an 203 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{203} nucleic acids; these proteins would have 99.5% identity to SEQ ID NO:2. Because nucleic acids with 85% identity to SEQ ID NO:2 could encode proteins with up

to 30 amino acid substitutions, many more than 19^{203} nucleic acids would need to be made and analyzed.

Decreasing the expression of a protein, for example by antisense suppression, is unpredictable. Arndt et al (1997, Genome 40:785-797) teach that the ability of an antisense construct to inhibit RNA expression is dependent on the rate of transcription of the antisense RNA relative to that of the sense RNA, the localization of the antisense gene in the genome, and the length of complementarity between the sense and antisense RNA; in addition, the effect of the latter varies from gene to gene and organism to organism (pg 787, left column).

Antisense constructs that are not completely homologous to the target gene can have very unpredictable effects. Colliver et al (1997, Plant Mol. Biol. 35:509-522) showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with *increased* levels of chalcone synthase transcripts (pg 519, left column, paragraph 2) and note other instances when this phenomenon has occurred (pg 519, right column, paragraph 1).

As the specification does not describe the transformation of any plant with a nucleic acid with 85% identity to SEQ ID NO:1 or 3, a nucleic acid comprising 20 contiguous nucleotides of SEQ ID NO:1 or 3, or a nucleic acid that hybridizes to SEQ ID NO:1 or 3, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with altered disease resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled.

8. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing

subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to nucleic acid(s) in Patent Deposit No. PTA-1688. Since the nucleic acid(s) are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmids are not so obtainable or available, a deposit of microorganism containing said nucleic acid(s) may satisfy the requirements of 35 USC 112. The specification does not disclose a repeatable process to obtain the nucleic acid(s) and it is not apparent if the nucleic acid(s) are readily available to the public. Thus, a deposit is required for enablement purposes.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

9. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that have 85% identity to SEQ ID NO:1 or 3, that comprise 20 contiguous nucleotides of SEQ ID NO:1 or 3 or that hybridize to SEQ ID NO:1 or 3. In contrast, the specification only describes a coding sequence from maize that comprises SEQ ID NOs:1 and 3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Additionally, the claims, with the exception of claim 1, part (c), and claim 10, part (iii), do not describe the function of the protein encoded by the nucleic acid. The activity described in claim 1, part (c), and claim 10, part (iii), "PC1-C10-like activity" is not described by the specification.

Hence, Applicant has not, in fact, described DNA molecules that have 85% identity to SEQ ID NO:1 or 3, that comprise 20 contiguous nucleotides of SEQ ID NO:1 or 3 or that hybridize to SEQ ID NO:1 or 3 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1 and 10 are indefinite in their recitation of "the cDNA insert of Patent Deposit No. PTA-1688" in parts (c) and (iii), respectively. It is unclear what is in Patent Deposit No. PTA-1688 or what portion of any nucleic acid(s) in the deposit is the cDNA insert.

Claims 1 and 10 are indefinite in their recitation of "PR1-C10-like activity" in parts (c) and (iii), respectively. The term has no meaning in the art, and is not defined in the specification. Pg 39, lines 27-29, of the specification provides examples of PC1-C10 like activity, but that activity is not defined. Additionally, it is not clear how "PR1-C10-like activity" differs from PR1-C10 activity.

Claims 1 and 10 are indefinite in their recitation of "high stringency conditions" in parts

(c) and (v), respectively. It is not clear what hybridization and wash conditions constitute high stringency conditions.

Claim 8 is indefinite in its recitation of "Transformed seed". It is unclear what the seed was transformed with. Note that not all seeds of a transformed plant will have the DNA with which the parent plant was transformed. If Applicant wishes to indicate that the seed has the vector with which the parent plant was transformed, it is suggested that the claim be amended to state that the seed comprises the vector.

Claim 10, part (vii) lacks antecedent basis for the limitation "polynucleotide of a), b), c), d), e) or f)" as there is no such polynucleotide in the claim. The polynucleotides are under parts (i)-(vi) in claim 10.

Claim 10 is indefinite in its recitation of ""inducing the expression" in part (c). It is unclear what is done to induce the expression, as the promoter in part (a) is not an inducible promoter.

Claims 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The methods are ones of modulating the level of PR1-C10 polypeptide in a plant. However, the only method steps involve plant cells. Part (b) of claim 10 cultures the plant cell under plant growing conditions, but a plant is not regenerated and a plant is not used in step (c). The omitted steps are those involved regenerating the plant cell into a plant. Alternately, the method should be one of modulating the level of PR1-C10 polypeptide in a plant cell.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Ryals et al (WO 95/19443).

Ryals et al teach an isolated nucleic acid that comprises a region of 31 nucleotides with 90.3% identity to SEQ ID NO:1 and 3 and that would hybridize under "high stringency conditions" to SEQ ID NO:1 (see sequence search results). Ryals et al also teach a vector comprising the nucleic acid (pg 44, paragraph 2); this vector is one for making cDNA libraries and that vector would be in host cells in at least some point in the construction of the library.

14. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Bloksberg et al (1998, US Patent 5,850,020).

Bloksberg et al teach isolated an nucleic acid that comprises 42 contiguous bases of SEQ ID NO:1, recombinant expression cassettes comprising the nucleic acid operably linked to a promoter, vectors comprising the nucleic acid, and cells comprising the vector (column 9, line 44, to column 10, line 12). Bloksberg et al also teach plant cells, plants and seeds transformed with the nucleic acid (claims 15-19); Bloksberg et al also teach methods of plant transformation that require vectors (column 7, lines 46-56) and teach the transformation of the nucleic acid into maize, wheat and barley (column 7, lines 21-23).

The nucleic acid taught by Bloksberg et al encodes cinnamoyl-CoA reductase (column 10, line 11), an essential enzyme in the production of lignin (Figure 1). Bloksberg et al teach

that lignin plays a role in disease resistance (column 1, lines 21-23). The instant specification, on pg 39, lines 27-29, teaches that PR1-C10 like activity includes participation in the enhancement of disease resistance. Thus, the methods taught by Bloksberg et al of producing a plant with altered lignin structure and of modifying the activity of the enzyme (claims 32 and 37) would inherently be ones of modulating the level of PR1-C10 protein in a plant. The steps of the methods of Bloksberg et al and the claimed method are identical; induction of the expression the polynucleotide transformed into the plants must inherently happen to alter lignin structure or modify the activity of the enzyme.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
March 20, 2003